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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/664,432	09/19/2003	Charles E. Hart	00-12D1	5728

10117 7590 08/22/2007.

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EXAMINER	
JIANG, DONG	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
08/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/664,432	HART ET AL.	
	Examiner	Art Unit	
	Dong Jiang	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2-9,11 and 22-25* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-9,11 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's amendment filed on 04 June 2007 is acknowledged and entered. Following the amendment, claims 12, 13 and 26 are canceled, and claims 6, 11, 22 and 24 are amended.

Currently, claims 2-9, 11 and 22-25 are pending and under consideration.

Withdrawal of Objections and Rejections:

All objections and rejections of claims 12, 13 and 26 are moot as the applicant has canceled the claims.

All prior art rejections made in the last Office Action are withdrawn in view of applicant's argument and amendment.

Rejections Over Prior Art:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2-5, 7-9, 11, 22, 23 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al., US6,455,283 B1 (provided by applicants).

Ferrara discloses a human vascular endothelial growth factor, VEGF-E, which amino acid sequence of SEQ ID NO:2 is 100% identical to the present SEQ ID NO:2, and can form hetero- and homodimers (column 26, lines 16-17). Additionally, Ferrara teaches VEGF-E variants including one or more amino acid residues are added, deleted, or substituted at the N- or C-terminus or within the sequence as well as *active fragments* thereof (column 8, lines 15-24). Further, Ferrara teaches that VEGFE may be used to stimulate wound healing or tissue regeneration and associated therapies connected with regrowth of tissues such as, among others, connective tissue, skin, bone, cartilage (column 42, lines 21-25), and would be useful for indications where angiogenesis is desired such as, among others, osteoporosis (column 43, lines 8-17), and has application in the healing of bone fractures and cartilage damage or defect in humans or other animals (column 44, lines 49-53). Furthermore, Ferrara teaches that VEGF-E can be formulated to prepare pharmaceutically-useful compositions by mixing with a pharmaceutical acceptable carrier vehicle (column 46, lines 57-61), such as, among others, hydrophilic polymers (column 47, line 36), and that potential matrices for the compositions include, among others, tricalcium phosphate (column 50, lines 57-59). Furthermore, Ferrara teaches that for compositions that are useful for bone, cartilage, tendon, or ligament regeneration, the therapeutic method includes administering the composition systemically, or locally as an implant or device, and that preferably, for bone and/or cartilage formation, the composition would include a matrix capable of delivering the composition to the site of bone and/or cartilage damage (column 50, lines 36-39 and 45-48). Furthermore, Ferrara teaches that de novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma-induced, or oncologic, resection-induced defect (column 44, lines 57-60), and combination therapies, wherein VEGF-E can be combined with other growth factors such as, among others, IGF and PDGF, for promoting cell proliferation, survival, differentiation, and repair (column 52, lines 36-41).

Ferrara does not explicitly mention a homodimer of VEGF-E, wherein each chain consisting of residues X-345, and X is an integer from 226-235.

However, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make the composition comprising the homodimer of the polypeptide fragments as defined in the instant claims and a pharmaceutically acceptable delivery vehicle

based on the sequence of VEGF-E taught by Ferrara, to combine the composition with other growth factors such as IGF or PDGF for the treatment of a patient suffering from, for example, bone (fracture, for example) and/or cartilage damage, and osteoporosis with the composition for promoting growth of bone or cartilage, as indicated by Ferrara. The person of ordinary skill in the art would have been motivated to do so for disease treatment such as arthritis (cartilage damage) and osteoporosis, and reasonably would have expected success because Ferrara teaches that VEGF-E is useful for bone, cartilage, tendon, or ligament regeneration. With respect to the limitation "stimulating proliferation of osteoblasts or chondrocytes" in claim 22, it would be an inherent property of the method for promoting growth of bone, ligament, or cartilage (claim 11, for example).

Claims 6 and 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ferrara et al., US6,455,283 B1, as applied to claims 2-5, 7-9, 11, 22, 23 and 25 above, and further in view of Bentz et al., EP 0 512 844 A1.

The teachings of Ferrara are reviewed above. The reference does not explicitly teach covalently linking the VEGF-E to a bone-targeting agent.

The teachings of Bentz were reviewed in the last Office Action. Briefly, Bentz teaches a composition comprising a bone growth factor and a bone-targeting agent, and a method of use thereof for augmenting bone formation or treating bone defects or bone loss, and for bone repair in a subject (column 4, lines 29-44, and column 7, lines 50-52). Further, Bentz teaches that targeted delivery of bone growth factors may reduce harmful or undesirable effects of those molecules, allow the use of lower doses because relatively higher doses can be delivered to the site of interest, and prolong the effect, and that a targeting molecule that influences bone metabolism may result in an additive or synergistic effect (column 4, lines 18-25).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to link the VEGF-E taught by Ferrara to a bone-targeting agent such as those taught by Bentz for bone repair or treating bone defects or bone loss because targeted delivery may reduce undesirable effects, allow the use of lower doses and prolong the effect, and may result in an additive or synergistic effect, as indicated by Bentz. The person of ordinary skill in the art would have been motivated to do so for bone disease treatment, and for the advantages of

targeted delivery as taught by Bentz, and reasonably would have expected success because Ferrara teaches that VEGF-E is useful for bone, cartilage, tendon, or ligament regeneration, and Bentz has successfully demonstrated the conjugations comprising a bone growth factor and a bone-targeting agent.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Dong Jiang

Dong Jiang, Ph.D.
Patent Examiner
AU1646
8/18/07